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| 10/618,531 | 07/11/2003 | Philip A. Furman | 04674.105074 (TRI 1016) | 6903 |

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| EXAMINER | |
|---|---|
| JAGOE, DONNA A | |
| ART UNIT | PAPER NUMBER |
| 1614 | |
| MAIL DATE | DELIVERY MODE |
| 08/16/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/618,531 | FURMAN, PHILIP A. | |
| | Examiner | Art Unit | |
| | Donna Jagoe | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants' arguments filed April 17, 2007 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

***Claims 1-8 are pending in this application.***

### *Claim Rejections - 35 USC § 102*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Schinazi et al. U.S. Patent No. 5,703,058 A.

Schinazi et al. teach FTC exhibits activity against Hepatitis B virus (HBV) (column 2, lines 40-41) and genetically engineered vaccine, alpha interferon effective for HBV (column 2, lines 46-55). Schinazi et al. further disclose that L(-)FMAU is another example of an antiviral agent that can be used in combination with the (-) enantiomer of FTC (column 6, lines 21-27) for the treatment of HBV infections in humans (column 3, lines 5-6).

***Claim Rejections - 35 USC § 103***

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schinazi et al. U.S. Patent No. 5,703,058 A and Thyagarajan U.S. Patent No. 6,589,570 B1.

Schinazi et al. teach FTC exhibits activity against Hepatitis B virus (HBV) (column 2, lines 40-41) and genetically engineered vaccine, alpha interferon effective for HBV (column 2, lines 46-55). Schinazi et al. further disclose that L(-)FMAU is an example of an antiviral agent that can be used in combination with the (-) enantiomer of FTC (column 6, lines 21-27) for the treatment of HBV infections in humans (column 3, lines 5-6)..

Schinazi et al. does not teach the $\beta$-L-FTC is substantially pure and it does not teach the many variations of interferon.

In general, stereoisomers/optical isomers are obvious from racemic mixtures. As legal authority the examiner cites *In re Adamson and Duffin,* 125 U.S.P.Q. 233. The case sets forth the requirements of patentability with regard to stereoisomers as follows:

1) The existence of a racemate is, in and of itself, sufficient to render obvious any individual stereoisomers contained within; no express suggestion of isomer separation is needed. See the first paragraph on page 235.

2) One skilled in the art expects that individual stereoisomers will differ significantly in physiological/pharmacological activity and toxicity, because living systems are chiral and thus preferentially process stereochemical configurations over

others. See page 234, the third full paragraph and page 235, the fifth full paragraph on the page.

L-FTC is known from the recitation of its use for treatment of HBV in U. S. Patent 5,703,058. Consonant with the reasoning of *Adamson*, the existence of that racemate renders obvious any individual stereoisomers contained within, i.e. the R and S enantiomers recited instantly. Regarding the substantially pure form of β-L-FTC, Schinazi et al. teach that the β-L forms are specifically contemplated (column 7, line 64 to column 8, line 3). Schinazi teach that enantiomerically pure forms are used herein and the term enantiomerically enriched refers to a nucleoside composition that includes at least 95% to 98% of a single enantiomer of that nucleoside (column 6, lines 45-49). One skilled in the art would have been motivated to prepare additional useful compositions of the ranges taught by the prior art. While the reference is silent regarding the 90% by weight ratios, the difference in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. When the general conditions are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 45, 105 USPQ 233, 235 (CCPA 1955). In the absence of any criticality and/or unexpected results of the additional ranges claimed, the instant invention is considered obvious.

Regarding the method of use of alpha, beta and gamma interferon for the method of treating hepatitis B, Thyagarajan (quoting Lau et al., Gut. Suppl. 1991;547-562) recites in Table 1 (column 2), agents that have been studied and are successful in

the treatment of HBV infection are *inter alia* Interferons such as Alpha interferon, Beta interferon and Gamma interferon.

It would have been made obvious to one of ordinary skill in art at the time it was made to employ the combination of β-L-FTC and L-FMAU and interferon for the treatment or prophylaxis of a human infected with hepatitis B virus motivated by the teaching of Schinazi et al. who recites that L(-)FMAU is an example of an antiviral agent that can be used in combination with the (-) enantiomer of FTC (column 6, lines 21-27) for the treatment of HBV infections in humans (column 3, lines 5-6) along with alpha interferon (column 2, lines 46-55) and the teaching of Thyagarajan who recites that Interferons such as Alpha interferon, Beta interferon and Gamma interferon are successful treatments for HBV.

***Response to Arguments***

Applicant asserts that Schinazi does not disclose the combination or alternation of the three components with each other. In response, the claim recites a composition that is in combination with β-L-FTC, L-(-) FMAU and interferon. The word "and" in line 12 of the claim denotes that the agents are used in combination with each other. Further, the claim language *comprising* leaves the claim open for the inclusion of unspecified ingredients, even in major amounts and as such, does not exclude the composition of claim 1.

Applicant asserts that Schinazi does not teach a method for the treatment or prophylaxis of a human infected with hepatitis B virus comprising administering in combination or in alternation an effective amount of β-L-FTC, L-FMAU and Interferon. In response, the claim recites a composition that is in combination with β-L-FTC, L-(-) FMAU and interferon. The word "and" in line 12 of the claim denotes that the agents are used in combination with each other. Further, the claim language *comprising* leaves the claim open for the inclusion of unspecified ingredients, even in major amounts and as such, does not exclude the composition of claim 1.

Applicant asserts that the examiner has mischaracterized the teaching of Thyagarajan and states that the reference teaches away from the use of interferons. In response, applicant is directed to the sentence directly below table one in column 2 of the reference wherein it is stated that "except the interferons, lamuvidine and the latest entry Phyllanthus amarus, the others seem to be far from successful." In other words agents other than those stated are not successful in the treatment of Hepatitis B, but the interferons are successful. Thyagarajan only states that the problem with the interferons and lamuvidine is the non-accessibility in third world countries.

## *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 9:00 A.M. - 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe
Patent Examiner
Art Unit 1614

August 10, 2007

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER